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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,690	04/26/2005	Kirvin L. Hodge	18028-PCTUS	5946

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LEWIS J. KREISLER
LEGAL DEPARTMENT
930 CLOPPER ROAD
GAITHERSBURG, MD 20878

EXAMINER	
ZHANG, NANCY L	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 12/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/532,690	HODGE ET AL.	
	Examiner	Art Unit	
	Nancy L. Zhang	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2-9 is/are pending in the application.

4a) Of the above claim(s) 9 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 2-8 is/are rejected.

7)☒ Claim(s) 8 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 2-8, drawn to a method of treatment comprising administering an agent selected from the group consisting of the agents in claim 2.

Group II, claim 9, drawn to a pharmaceutical composition comprising a biologically active agent selected from the group consisting of the agents in claim 9.

The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The common technical feature shared among the above groups is a compound of the list in claim 2. This element cannot be a special technical feature under PCT Rule 13.2 because the compounds as listed in claim 2 are known compounds (admitted in applicant's specification, page 9, line 19). Therefore, inventions in Groups I and II are not unified by a special technical feature. Since Applicant's inventions do not contribute a special technical feature when viewed over the prior art they do not have a single general inventive concept and so lack unity of invention.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1. Under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: each of the compounds is a separate molecular entity requiring a different field of search.

Applicant is required to elect a single disclosed species under the elected subgenus group, for example, a specific compound from the list in claim 2 such as 4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the

requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Election

During a telephone conversation with Mr. Lewis Kreisler on 11/13/2006, a provisional election was made with traverse to prosecute the invention of Group II, claims 2-8, along with the compound of 4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid as the elected species. Affirmation of this election must be made by applicant in replying to this Office action. Claim 9 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim 9 is withdrawn from consideration because it is not directed to the elected invention.

Claims 2-8 are examined.

Claim Objections

Claim 8 is objected to because of the following informalities: the incorrect use of a Markush group. The use of a colon is not needed. A Markush group should have the word "and" between the last two recited items. Appropriate correction is required.

Lack Scope of Enablement Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing blood glucose, triglycerides and fatty acids level in diabetic mice using the compounds listed in claim 2, does not reasonably provide enablement for treating all of the diseases listed in claim 2 using any of these compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in ***In re***

Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: the nature of the invention; the state of the prior art; the relative skill of those in the art; the predictability or unpredictability of the art; the breadth of the claims; the amount of direction or guidance presented; the presence or absence of working examples; and the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The present invention are drawn to a method for treating insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis by administering to a mammalian subject an active agent as listed in claim 2.

The specification only discloses working examples of anti-diabetic effects for reducing blood glucose, triglycerides and fatty acids level by the administration of the compounds of claim 2 to diabetic mice.

It is generally recognized in the art that biological compounds often react unpredictably under different circumstances (Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970)). The relative skill of the artisan or the unpredictability of the pharmaceutical art is very high. Where the physiological activity of a chemical or biological compound is considered to be an unpredictable art (Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of

unpredictability of the factors involved" (See In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970)), the skilled artisan would have not known how to extrapolate the results provided in the instant specification to the larger and varied genus of treatment of all of the disorders including insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis. For example, cachexia is characterized by progressive weakness, dramatic weight loss and wasting and is a common condition arising in many human cancer patients (Tisdale et al., US Patent 5,219,579, issued Jun. 15, 1993, column 1, lines 26-28). The specification of the instant application has not provided guidance, working example or mechanisms of action for the treatment of cachexia using the compounds listed in claim 2.

The examiner acknowledges that the Office does not require the presence of working examples to be present in the disclosure of the invention (see MPEP 2164.02). However, given the highly unpredictable state of the art and furthermore, given that the applicant does not provide sufficient guidance or direction as to how to make and use the full scope of the instant claimed invention without undue amount of experimentation, the Office would require appropriate disclosure, in the way of scientifically sound reasoning or the way of concrete examples, as to why the data shown is a reasonably representative and objective showing such that it was commensurate in scope with and, thus, adequately enables, the use of these compounds for the full scope of the presently claimed subject matter. In the absence of such guidance and evidence or reasoning, the specification fails to provide an enabling disclosure.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

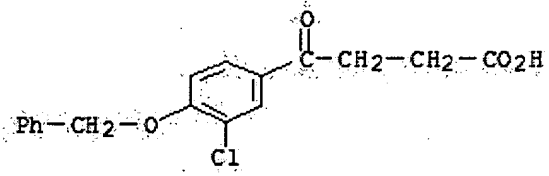
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

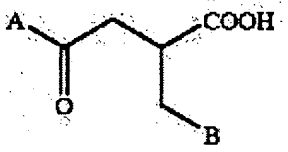
Claims 2-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moinet et al. (US Patent 6,143,787, issue date: Nov. 7, 2000).

The invention of claims 2-8 is directed to a method for treating insulin resistance syndrome, diabetes, hyperlipidemia, fatty liver disease, cachexia, obesity, atherosclerosis and arteriosclerosis comprising administering to a mammalian an active agent such as 4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid. Further limitations include the agent is administered orally (claim 3); the subject is a human (claim 4); the amount of agent is 1 mg to 400 mg per day and the specific diseases of treatment

(claims 6-7). The structure of 4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid is as follows:



Moinet et al. disclose pharmaceutical composition containing 4-oxobutanoic acids useful in the treatment of diabetes (column 1, lines 4-6). Moinet et al.'s compounds have the structure of formula (I):



(I)

in which the groups A and B are chosen, independently of each other, from:
a mono-, bi- or tricyclic aryl group having from 6 to 14 carbon atoms;
a heteroaromatic group chosen from pyridyl, pyrimidyl, pyrrolyl, furyl and thienyl groups;
an alkyl group having from 1 to 14 carbon atoms;
a cycloalkyl group having from 5 to 8 carbon atoms;
a saturated heterocyclic group chosen from tetrahydrofuryl, tetrahydropyranyl, piperidyl and pyrrolidinyl groups;
to its solvate or to a salt of this acid with a pharmaceutically acceptable base.

The base structure of formula (I) is the same as the base structure of the compound 4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid of the instant application.

Moinet et al.'s disclosure differs from the instant claimed invention in that Moinet et al. fail to disclose that

(i) the compound being used in the treatment is the 4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid where the branch group of B at 2-position of oxobutanoic acid is absent and the substituents on the 4-aryl group is modified; and

(ii) the mammalian subject for the treatment is a human.

However, since the Group B of formula (I) can be an alkyl group of 1-14 carbon atoms (column 1, line 24), the substitution of an alkyl group with hydrogen at the 2-position of oxobutanoic acid is obvious. In addition, since the Group A of formula (I) can be an aryl group bearing 1-3 substituents such as an aryl-alkyl group and halogen (column 1, lines 34-35), the modification of Group A being a benzyloxy-chloro-phenyl is obvious. Therefore, one having ordinary skill in the art would have been motivated at the time of the instant invention to modify the compound of formula (I) with the above mentioned substituents to result in the compound 4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid of the instant invention with the expectation that the substitution would not significantly alter the analogous properties of compounds of the prior art due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055.

With respect to the mammalian subject being treated is a human, Moinet et al. teach a method for treating diabetes comprising administering to a patient a composition of formula (I) (column 20, lines 43-44) and the treatment shows no sign of toxicity (column 17, lines 56-57). One having ordinary skill in the art would have been

motivated at the time of the instant invention to practice Moinet et al.'s method of treating diabetes on a human patient.

Therefore, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify Moinet et al.'s compound of formula (I) and practice the method of treatment to result in the practice of the instant invention with a reasonable expectation of success.

With respect to claim 3 wherein the agent is administered orally, Moinet et al. disclose that the composition may be provided in forms intended for oral administration (column 3, lines 64-65).

With respect to claim 5 wherein the amount of agent administered is 1 mg to 400 mg, Moinet et al. disclose that the products were administered orally at a dose of 200 mg/kg (column 17, lines 56-57).

With respect to claim 6 wherein the disease condition is insulin resistance syndrome or type II diabetes (insulin-independent diabetes), Moinet et al. disclose that the composition may be used in the treatment of diabetes, in particular insulin-independent diabetes (column 3, lines 59-61).

With respect to claim 7 wherein the disease condition is type I diabetes (insulin-dependent diabetes), Moinet et al. teach a method for treating diabetes comprising administering to a patient a composition of formula (I) wherein the diabetes is insulin-dependent diabetes (column 20, lines 46-47).

With respect to claim 8, the recitation of the effects of a treatment does not limit the method because there is no additional step in the claimed method to test the results of treatment. Thus this recitation is viewed as the property of the method of treatment.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-13 of copending Application No. 10/553,936, claims 6-13 of copending Application No. 10/531,618. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

With respect to claims 6-13 of copending Application No. 10/553,936, the base structure of formula (I) is the same as the base structure of the compounds such as 4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid of the instant application. Furthermore, the physiological activities are analogous. The only difference is that there is a keto group adjacent to the benzene ring on the carbon chain of the alkyloic acids of the instant application whereas there is a double bond instead of a hydroxyl group at the same position in the formula of the copending application. However, the substitution of keto groups with alkenyl groups is obvious. One having ordinary skill in the art would have been motivated to substitute the hydroxyl group with a double bond with the expectation that the substitution of a keto group for a double bond would not significantly alter the analogous properties of the compound due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055.

With respect to claims 6-13 of copending Application No. 10/531,618, the base structure of formula (I) is the same as the base structure of the compounds such as 4-(4-benzyloxy-3-chlorophenyl)-4-oxobutanoic acid of the instant application. Furthermore, the physiological activities are analogous. The only difference is that there is a keto group adjacent to the benzene ring on the carbon chain of the alkyloic acids of the instant application whereas there is a hydroxyl group at the same position in the formula of the copending application. However, the substitution of keto groups with hydroxyl groups is obvious. One having ordinary skill in the art would have been motivated to substitute the keto group with a hydroxyl group with the expectation that the substitution would not significantly alter the analogous properties of the compound

due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

In looking in continuity data, it is noted that applicant has numerous copending applications encompassing the same or similar subject matter of the instant application, for example, claims 1-44 and 46-66 of copending application 11/535,779. Applicant should review all subject matter considered the same or similar and submit appropriate Terminal Disclaimer(s).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy L. Zhang whose telephone number is (571)-272-8270. The examiner can normally be reached on Mon.- Fri. 8:30am - 5:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

nlz 12/5/06

NLZ

BRIAN-YONG S. KWON
PRIMARY EXAMINER